REMARKS/ARGUMENTS

Elected Invention

In light of the Examiner's decision to withdraw claims 3, 8-16 and 35-38, Applicant reserves the right to pursue the subject matter of the withdrawn claims in a divisional application without prejudice or disclaimer.

Priority

The Examiner has rejected the priority claim of the present application to PCT/CA99/00314, filed 4/7/99, alleging that the disclosure of the invention in the priority (i.e. parent) application and in the later-filed (present) application must be sufficient to comply with 35 USC §112, 1st paragraph, otherwise the later-filed application does not comply with the conditions set forth under 35 USC §120. In particular, the Examiner states the following:

> "A review of PCT/CA99/00314 as filed did not reveal a description of the claimed invention drawn to a modified IRF protein ... with the proviso that where said IRF protein is IRF-3, said at least one modified phosphoacceptor site does not comprise Ser-385 or Ser-386. There is no description of the modified IRF proteins having this particular limitation or that the specification set[s] [sic] forth a description that modified IRF-3 having either specific modification is known in the prior art (and thus the limitation excluding known prior art can be added without adding new matter)."

Without acquiescing to the Examiner's position and merely to advance prosecution, former claim 1 has been cancelled which renders the rejection moot concerning the priority claim of the present application to PCT/CA99/00314. In addition, claims 2, 27 and 33 have been cancelled and a new claim 39 has been added which finds support throughout the description and in the examples.

Support for the Proviso

Applicant respectfully disagrees that the priority Application PCT/CA99/00314 does not provide a description of the modified IRF proteins having the limitation stated above or that modification to Ser-385 or Ser-386 is not known in the art. On this point, Applicant refers to the Example in the description entitled "Mapping the IRF-3 Phosphorylation Sites" at page 25, lines 23 to 28 where it states the following:

> "Another study suggested the involvement of the Ser residues at aa385 and 386 as potential phosphoacceptor sites (67). However, in studies with the S385A/S386A mutation, no evidence was found for inducible phosphorylation at these sites."

> [(67) Yoneyama, M. Suhara, W., Fukuhara, Y. and Fujita, T. 1997. Direct activation of a factor complex composed of IRF-3 and CBP/p300 by virus infection. J. Interferon Cytokine Res. 17:S53]

35 USC §112, 1st paragraph

Furthermore, Applicant respectfully disagrees that compliance with 35 USC §112, 1st paragraph has not been met. The test for determining compliance with the written description requirement under 35 USC §112, 1st paragraph is whether the disclosure of the application as originally filed reasonably conveys to the artisan that *the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language.* [Emphasis added.] ***In re Kaslow***, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983).

> "The function of the description requirement [of the 1st paragraph of 35 USC §112] is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." ***In re Wertheim***, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). "It is not necessary that the application describe the claim limitations exactly, ... but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented processes including those limitations." ***In re Wertheim, supra*** citing ***In re Smythe***, 480 F.2d 1376, 1382, 178 USPQ 279, 284 (CCPA 1973).

Thus, case law has repetitively stated that "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; *how* the specification accomplishes this is not material." [Emphasis added.] *Wertheim*, 541 F.2d at 262, 263 (C.C.P.A. 1976).

> "To rule otherwise would let form triumph over substance, substantially eliminating the right of an applicant to retreat to an otherwise patentable species merely because he erroneously thought he was first with the genus when he filed. Cf. (citation omitted). Since the patent law provides for the amendment during prosecution of claims, as well as the specification supporting the claims, 35 USC §132, it is clear that the reference to "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention" in the 2nd paragraph of 35 USC §112 does not prohibit the applicant from changing what he "regards as his invention" (i.e., the subject matter on which he seeks patent protection) during the pendency of his application." Cf. (citation omitted).

The CCPA soon had occasion to apply the above in *In re Johnson*, holding that a claim to a genus with a recital of a negative proviso that did not appear in the specification complied with the description requirement. The negative proviso had the effect of excluding from the scope of

the claim two species originally disclosed in the specification as within the invention, and was inserted to avoid having the claims read on a lost interference count. 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977).

The court stated:

> "The notion that one who fully discloses and teaches those skilled in the art how to make and use a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements 35 USC §112, 1st paragraph, appears to result in hypertechnical application of legalistic prose relating to that provision of the statute. 558 F.2d 1019, 194 USPQ 196 (CCPA 1977)."

In view of the above, Applicant respectfully submits that a rejection of the priority claim for lack of compliance with 35 USC §112, 1st paragraph is unfounded. The Examiner has not established a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed.

Drawings

The drawings page 7/30 containing Figures 5a to 5h has been objected to for containing color photographs. Accordingly, Applicant submits a new drawings page containing black and white photographs labelled as Figures 5a to 5h.

Specification

The abstract has been objected to for not beginning on a separate page and therefore, a new abstract is submitted herewith which complies with U.S. patent practice.

Claim Objections

Claims 19 to 21 of record are objected to for being in improper multiple dependent form.

The multiple claim dependency of claim 19 to "claims 6 or 7" has been amended to depend only from claim 6. The objection to claims 20 and 21 is believed to be avoided by virtue of their dependency to amended claim 19 which is now in proper dependent form under U.S. patent practice.

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Claim Rejections - 35 USC §112

Claims 26 to 27 and 32 to 34 of record stand rejected for an alleged lack of enablement in the description relating specific uses of the claimed pharmaceutical composition to treatment a number of diseases.

Claims 26 and 32 have been amended by removing the phrase "for the treatment of a viral infection" and claim 34 has been amended to remove the phrase "for the treatment of cancer". Claims 27 and 33 have been cancelled.

Claim Rejections - 35 USC §101

Claims 1 to 2, 4 to 5 and 17 to 18 of record stand rejected for allegedly claiming non-statutory subject matter, namely a product of nature.

Claims 1 and 2 have been cancelled which renders the rejection moot thereto.

Claims 4 to 5, 17 to 18 and dependent claims thereon have all been amended to define the interferon regulatory factor as "isolated".

Claim Rejections - 35 USC §102

The Examiner has applied Sharf *et al.*, Yoneyama *et al.*, Zhang *et al.*, Au *et al.*, Lin *et al.*, or Hiscott *et al.* alleging that on separate issues, the subject matter of claims 1 to 2, 4 to 7, 17 to 18, 26 to 27 and 32 to 34 of record is anticipated by any one of these references under 35 USC §102(b).

Claims 1 and 2 have been cancelled which renders the rejection moot thereto. The remaining claims have been amended to depend upon new claim 39 which finds support throughout the description and the examples.

MPEP §2131 provides that:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The **identical invention** must be shown in as complete detail as contained in the ... claim." [Emphasis added.] *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

MPEP §2121.01 also provides that:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102 the stated test is whether a reference contains an **'enabling disclosure'** ... ." *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). [Emphasis added.] A reference contains an enabling disclosure if the public was in possession of the claimed invention before the date of the invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Applicant respectfully disagrees that the claimed subject matter is anticipated by the cited references and addresses each reference with comments in respect thereof.

Claims 1, 2 and 5 - Sharf et al.

This reference discloses a different member of the IRF family, namely ICSBP. This protein as described in Scharf *et al.* is ***modified by tyrosine phosphorylation*** and not by serine or threonine phosphorylation. Furthermore, this protein behaves very differently from IRF3 in that:

- it is expressed only in lymphoid and myeloid cells; and
- it acts as a repressor and therefore, removing the carboxy-terminal end of ICSBP results in an increase in cytokine gene activation because its ability to repress gene expression is removed.

The Examiner also states that "this reference also teaches IRF1 is phosphorylated in response to IFN treatment". However, while IRF1 may be phosphorylated in response to IFN treatment, the nature of the phosphoacceptor sites is not known, nor is it known whether the phosphorylation occurs in the carboxy-terminal portion of the protein or in other regions of the protein.

Claims 1, 2 and 5 - Yoneyama et al.

The results of the Yoneyama *et al.* reference may be summarized as follows. IRF-3 becomes serine-phorphorylated upon viral induction, which correlates with an increase in IFN gene expression. It was also shown that the deletion of carboxy-terminal residues 375-427 results in no inducible phosphorylation or transactivation. Therefore, Yoneyama *et al.* proceeded to perform a mutational analysis on six of the seven serine residues contained in this region, i.e. residues 385, 386, 396, 398, 402 and 405. The results of these experiments revealed that only Ser-385 and Ser-386 were responsible for the observed effects, since these point mutants behaved the same as the carboxy-terminal 375-427 deleted version, while the remaining mutants "behaved essentially indistinguishably from the wild-type." In other words, Yoneyama *et al.* demonstrated the critical functionality of the serine residues at 385 and 386 when mutated to ***alanine residues*** generated an ***inactive version*** of the IRF3 protein that does not translocate to the nucleus to stimulate cytokine gene activation.

Investigation of the same serine residues by the inventor indicated that when Ser-385 and Ser-386 are substituted with aspartic acid (which is a serine-threonine phosphomimetic which makes the protein behave as if it was phosphorylated), IRF3 activation ***does nor*** occur. Based on these results, it was also concluded that IRF3 Ser385 and Ser386 are important in regulating IRF3 activity, but they are not critical residues required to generate a constitutively active form of IRF3. Confirmational analysis by the inventor showed that alanine substitutions of serine residues at 396 to 405 of IRF3 also inactivated the protein, but that substitutions with aspartic acid residues at these same positions created a constitutively active form (i.e. makes IRF3 behave like a phosphorylated protein).

Therefore, Yoneyama *et al.* do not describe a role for the modification of serine residues 396, 398, 402 and 405 in the ***activation of IFN expression*** nor do they mention threonine residues in their studies.

Claims 1, 2, 4, 5, 17 and 18 - Zhang et al.

Zhang *et al.* disclose that the IRF7 protein is induced transcriptionally by IFN treatment, i.e. the amount of protein increases as a result of IFN treatment. However, there is no discussion whatsoever concerning phosphorylation of IRF7 at phosphoacceptor sites. Moreover, the identification of important phosphoacceptor sites which are targeted for phosphorylation has to be determined experimentally.

Claims 1, 2 and 5 - Au et al.

Based on the results and conclusions reached by Au *et al.*, the authors determined that IRF 3 ***does not activate expression of interferon genes and other cytokine genes.*** For example, in the Abstract, it states that "Expression as a Gal 4 fusion protein does not activate expression ... indicating that this protein does not contain the transcription transactivation domain." Furthermore, in the discussion at the top of page 11661, Au *et al.* state that "Its (IRF3 expression) is not further stimulated by virus infection or IFN treatment."

Claims 1, 2, 5 and 7 - Lin et al.
Claims 1, 2, 5, 7, 26, 27, 32, 33 and 34 - Hiscott et al.

Applicant respectfully submits that in light of the cancellation of claim 1 and arguments provided above that the remaining claims be accorded the priority claim of PCT/CA99/00314, filed 4/7/99. On this basis, it is submitted that neither the Lin *et al.* reference, nor the Hiscott *et al.* reference are citable under 35 USC §102(b) against the claimed subject matter.

- The Lin *et al.* reference was published on May 5, 1998 which is less than 12 months before the International filing date of April 7, 1999.
- The Hiscott *et al.* reference was published on October 14, 1999 which is after the International filing date of April 7, 1999.

Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the forgoing, early favorable consideration of this application is earnestly solicited.

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, he is invited to contact Joy Morrow at (613) 232-2486.

Respectfully submitted,

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Date

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